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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/751,053	12/29/2000	Daniel W. Gil	D2919	8979

7590 07/10/2002

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EXAMINER	
RILEY, JEZIA	

ART UNIT	PAPER NUMBER
1637	9

DATE MAILED: 07/10/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/751,053	Applicant(s) GIL ET AL.	
	Examiner Jezia Riley	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-67 is/are pending in the application.

4a) Of the above claim(s) 18-21,23,24,35 and 45-67 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-17,22,25-34 and 36-44 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-67 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election of group I in Paper No. 7 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-17, 22, 25-34, 36-44 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a agent comprising a targeting component of formulae I-VII, does not reasonably provide enablement for any targeting component wherein said targeting component selectively binds at the alpha-2B or alpha-2B/alpha-2c adrenergic receptor subtype (s) as compared to the alpha-2A adrenergic receptor subtype. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described in *In Re*

Colianni, 195 USPQ 150 (CCPA 1977) and have been adopted by the Board Appeals and Interferences in *Ex Parte Forman,* USPQ 546 (BPAI 1986).

Among these factors are: the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the breadth of the claims, the amount of direction or guidance present, and the presence or absence of working examples.

Breadth of the claims:

The claims are broadly drawn to a an agent comprising a therapeutic component and a targeting component wherein the targeting component selectively binds at the alpha-2B or alpha-2B/alpha-2c adrenergic receptor subtype (s) as compared to the alpha-2A adrenergic receptor subtype . Said "Agent" is very broadly defined and no specific structure or examples have been given. Therefore this reads on a wide variety of compositions.

Amount of direction/guidance

A broad possible range for the "Agent" is possible and in order to enable the selection of "Agent" there is a need to set forth experimental procedure to be used. It is undue experimentation to prepare any "Agent", to determine the ones that would be used to selectively bind at the alpha-2B or alpha-2B/alpha-2c adrenergic receptor subtype (s) as compared to the alpha-2A adrenergic receptor subtype. This is clearly an invitation to experiment to select "Agent" to make it specific to instant claim 1 for example. These leave the entire work of finding "Agent" up to someone wishing to practice claim 1 which is undue experimentation. The specification gives no guidance to permit one of skill in the art to devise strategies for synthesis of the compounds as

claimed. One of ordinary skill in the art would not know how to make any components that comprise the components as broadly defined, and how to determine that such a compound would satisfactorily selectively bind at the alpha-2B or alpha-2B/alpha-2c adrenergic receptor subtype (s) as compared to the alpha-2A adrenergic receptor subtype.

Therefore given the unpredictability of the art and the lack of guidance in the specification, it is the Examiner's position that one skilled in the art could not perform the method of the claims as broadly recited without undue experimentation.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1-17, 25-28, 30-34, 36-44 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Foster et al. (5,989,545).

Foster et al. discloses a novel agent that is able to modify peripheral afferent function. The agent may inhibit neurotransmitter release from discrete populations of neurons, and thereby reduce, or preferably prevent, the transmission of afferent pain signals from peripheral to central pain fibres. The agent may be used in or as a pharmaceutical for the treatment of pain, particularly chronic pain.

A non-cytotoxic agent which binds to a peripheral sensory afferent which comprises a Targeting Moiety (TM) coupled to a modified clostridial neurotoxin in which the TM comprises a ligand to a cell-surface binding site present on a primary sensory

afferent and is capable of functionally interacting with a binding site causing a physical association between the agent and the surface of a primary sensory afferent; and the heavy chain (H-chain) of the clostridial neurotoxin is removed or modified by chemical derivatisation, mutation or proteolysis to reduce or remove its native binding affinity for motor neurons; and the light chain (L-chain) of the clostridial neurotoxin or a fragment thereof retains a protease activity specific for components of the neurosecretory machinery; the TM and the modified H-chain, if present, forming a molecule which introduces the L-chain or fragment thereof into the cytosol of a primary sensory afferent, thereby inhibiting the transmission of signals between a primary sensory afferent and a projection neuron by controlling the release of at least one neurotransmitter or neuromodulator from the primary sensory afferent. The clostridial neurotoxin component is obtained from botulinum neurotoxin selected from the group consisting of botulinum neurotoxin type A, botulinum neurotoxin type B, and botulinum neurotoxin type C. Surprisingly, by covalently linking a clostridial neurotoxin, or a hybrid of two clostridial neurotoxins, in which the HC region of the H-chain has been removed or modified, to a new molecule or moiety, the Targeting Moiety (TM), that binds to a BS on the surface of sensory neurons, a novel agent capable of inhibiting the release of at least one neurotransmitter or neuromodulator from nociceptive afferents is produced. A further surprising aspect is that if the L-chain of a clostridial neurotoxin, or a fragment of the L-chain containing the endopeptidase activity, is covalently linked to a TM which can also effect internalisation of the L-chain, or fragment thereof, into the cytoplasm of a sensory neuron, this also produces a novel agent capable of inhibiting the release of at

least one neurotransmitter or neuromodulator. The covalent linkages used to couple the component parts of the agent may include appropriate spacer regions. The TM provides specificity for the BS on the nociceptive afferent neuron. The TM component of the agent can comprise one of many cell binding molecules, including, but not limited to, antibodies, monoclonal antibodies, antibody fragments.

The claims have added functions which the prior art has not analyzed; but given the above 102 rejection analysis substantiating the basic characterization of the composition of the invention being the same as the reference, these added characteristics are presumed to be inherent in the prior art composition.

As it is pointed in *In re Fitzgerald* (205 USPQ), page 594, 2nd col., 1st full paragraph, supports the shifting of the burden of proof to the applicant that the instantly claimed invention is novel and unobvious over the prior art. Since both the prior art and the instant application prepare and use composition which appeared to be identical for treating pain. The prior art therefore suggests that the composition therein disclosed are effective in such therapy therefore suggesting the instant application under 35 U.S.C. § 103(a).

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jezia Riley whose telephone number is 703-305-6855. The examiner can normally be reached on 9:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Patent Analyst Monica Graves whose telephone number is 703-305-3002 or to the Technical Center receptionist whose telephone number is 703-308-0196.

July 8, 2002

JEZIA RILEY
PRIMARY EXAMINER